

We Claim:

Sub C'
1. In a cell population comprising dividing and quiescent cells, a method for substantially and selectively killing said dividing cells, said method comprising contacting said cell population under infective conditions with a replication competent adenovirus comprising a mutation in the E1A RB family member binding region of said adenovirus, and allowing sufficient time for said adenovirus to infect said cell population.

2. A method as described in claim 1 wherein said dividing cells are cancer cells.

10 3. A method as described in claim 2 wherein said dividing cells are endothelial cells.

4. A method as described in claim 3 wherein said quiescent cells are endothelial cells.

15 5. A method as described in claim 4 wherein said adenovirus mutation in E1A RB family member binding region of said virus is in the E1A-CR2 region.

Sub C'
6. A method as described in claim 5 wherein said mutation in the E1A-CR2 region comprises a deletion or substitution of one or more amino acids 122 through 129.

20 7. A method as described in claim 5 wherein said mutation in the E1A-CR2 region comprises a deletion or substitution of one or more amino acids 111 through 123.

8. A method as described in claim 5 wherein said adenovirus is dl922/947.

25 9. A method as described in claim 5 wherein said adenovirus is dl1107.

10. A method as described in claim 5 wherein said adenovirus is pm928.

30 11. In a cell population comprising dividing and quiescent endothelial cells, a method for killing said dividing endothelial cells with substantially less killing of said quiescent endothelial cells, said method comprising contacting said cell population under infective conditions with a replication competent adenovirus, said adenovirus comprising a mutation

in an E1A CR2 RB family member binding region of said adenovirus, and allowing sufficient time for said mutant adenovirus to infect said cell population, wherein said mutant adenovirus replicates to higher titers in said dividing cells than wild type adenovirus.

5 ~~12.~~ A method for substantially and selectively killing dividing endothelial cells and cancer cells compared to quiescent endothelial cells in a cell population comprising said three cell types, said method comprising contacting said cell population under infective conditions with a replication competent adenovirus comprising a mutation in an E1A RB family member binding region of said adenovirus, and allowing sufficient time for said
10 mutant adenovirus to infect said cell population.

13. A method as described in claim ~~12~~ wherein said dividing endothelial cells are microvascular endothelial cells.

15 14. A method as described in claim ~~13~~ wherein said adenovirus mutation comprises a mutation in the E1A-CR2 region.

~~15.~~ A method for controlling angiogenesis in an animal by killing dividing microvascular endothelial cells, comprising administering to said animal in need of said control a
20 replication competent adenovirus comprising a mutation in an E1A RB family member binding region of said adenovirus, and allowing sufficient time for said mutant adenovirus to infect said endothelial cells.

25 16. A method as described in claim ~~15~~ wherein said E1A RB family member binding region of said adenovirus is in the E1A-CR2 region.

17. A method as described in claim ~~16~~ wherein said mutation in the E1A-CR2 region comprises a deletion or substitution of one or more amino acids 122 through 129.

30 18. A method as described in claim ~~16~~ wherein said mutation in the E1A-CR2 region comprises a deletion or substitution of one or more amino acids 111 through 123.

19. A method as described in claim 16 wherein said adenovirus is dl922/947.
20. A method as described in claim 16 wherein said adenovirus is dl1107.
21. A pharmaceutical composition comprising a Rb binding site adenoviral mutant in a physiological solution.
- 5 22. A pharmaceutical composition as described in claim 21 wherein said adenoviral mutant is dl922/947.
23. A pharmaceutical composition as described in claim 21 wherein said adenoviral mutant is dl1107.
24. A pharmaceutical composition as described in claim 21 wherein said adenoviral mutant is pm928.
- 10 25. A composition comprising a Rb binding site adenoviral mutant with a negative selection agent operably linked to a promoter.
26. A composition as described in claim 25 wherein said mutant is dl922/947.
27. A composition as described in claim 25 wherein said mutant is dl1107.
- 15 28. A composition as described in claim 25 wherein said mutant is pm928.